DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS

JUNE 6, 2002

WASHINGTON, DC

Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on June 6, 2002 at Marriott Wardman Park Hotel in Washington, DC. The following individuals were present to contribute to the discussion.

ACET Members/Liaisons

Dr. Charles Nolan, Chair
Dr. Stephanie Bailey
Dr. David Cohn
Dr. Masae Kawamura
Dr. Charles Wallace
Dr. Amy Bloom (USAID)
Dr. Henry Blumberg (IDSA)
Ms. Sue Etkind (NTCA)
Dr. Anne Fanning (IUATLD)
Dr. James Pearson (APHL)
Dr. Gary Roselle (DVA)
Ms. Rachel Stricof (APIC)
Dr. Michael Tapper (SHEA)
Dr. Teresa Watkins-Bryant (HRSA)

Designated Federal Official

Dr. Ronald Valdiserri, Executive Secretary

CDC Representatives

Dr. Kenneth Castro, DTBE Director
Ms. Paulette Ford-Knights
Dr. Michael Lademarco
Dr. Scott NcNabb
Mr. Paul Poppe
Mr. John Seggerson
Dr. Gregory Wagner (NIOSH)

Guests

Dr. Denise Toney

Opening Session. Dr. Charles Nolan, the ACET Chair, called the meeting to order at 8:00 a.m. on June 6, 2002. He welcomed the attendees to the proceedings and opened the floor for introductions. He noted that this meeting takes place on the heels of a very successful World Congress meeting and enthusiasm for tuberculosis elimination is high in the United States and around the world.

Dr. Ronald Valdiserri, the ACET Executive Secretary, reminded attendees to be mindful of the fact that the meeting and all comments are a matter of public record. Members with a conflict of interest were asked to excuse themselves from the meeting. CDC expects members whose terms have expired to continue to serve until their replacements have officially been appointed. Dr. Valdiserri noted an agenda change because Dr. Patrick Chaulk was unable to attend

Update by the National Center for HIV, STD, and TB Prevention (NCHSTP). Dr. Valdiserri presented a brief update on some of the center level activities. Since the last ACET meeting in February, 2002, Dr. Jeffrey Koplan stepped down as Director of CDC. David Fleming, former Deputy Director, is currently the acting CDC Director and Julie Gerberding is Acting Deputy Director. Mike Osterholm, who is known by many of the meeting participants, has been asked to be Secretary Thompson's representative on bioterrorism issues at CDC. Announcement of a new CDC Director is expected soon.

Significant personnel changes have taken place in NCHSTP, Office of the Director. Mr. Bill Nichols, who previously worked at NCPS and NIP, is the new Associate Director for Management and Operations. Mr. Carmine Bozzi, who formally held that position, has taken a position in CDC's Global AIDS program. The Associate Director for Science, Dr. Jim Buehler, retired from the Public Health Service to work at Emory and an announcement for his position has been posted. Dr. Ester Sumartojo, the Deputy Associate Director for Science under Jim Buehler, is assuming the acting responsibilities. Dr. Valdiserri or Dr. Harold Jaffe can be contacted for further information on the Associate Director for Science position.

Dr. Valdiserri reviewed the 2002 Budget for NCHSTP. Of interest to ACET members is the TB program increase of $5.1 million in 2002. The President's budget for 2003 is for support at the same level. The STD and HIV budgets were also increased in 2002.

Not related to TB, but of interest to this group, the HIV/AIDS programs at CDC are undergoing audits by the Office of the Inspector General. The first audit is an analysis of the global AIDS program with a focus on determining how funds are allocated and expended. The second audit will examine how CDC, as an agency, takes 'overhead' from appropriated funds for HIV-AIDS. A third audit is looking at grantees' compliance with financial and performance reporting

requirements and grant performance expectations. A fourth audit is planned to determine whether CDC is following applicable laws, regulations, and other guidance in making funding decisions. These audits are focused on HIV-AIDS; however they indicate a heightened sense of accountability and performance in other federal programs as well.

Update by the Director of the Division of TB Elimination (DTBE).

Dr. Kenneth Castro's status report covered the following areas. During World TB Day, a special *Morbidity and Mortality Weekly Report* was issued with two articles on tuberculosis and "a boxed" announcement for the reader indicating it was World TB Day and highlighting some of the history of TB since its discovery 120 years ago. DTBE's goal is to make a complete slide set on a national TB trends available to national TB controllers at an upcoming meeting in Alexandria, Virginia.

Dr. Castro provided a breakdown of how the extra $5 million FY2002 funds are being spent. The first action item was to fund a full complement of TB Epidemiology Studies Consortia as ACET members had requested at the previous meeting. In highlighting all the activities that are taking place, Dr. Castro noted this is a contractual agreement; therefore very specific product-oriented tasks are going to be implemented through the consortia. DTBE has initiated some low-incidence projects promulgated by a publication of an *MMWR* article barely a month ago and will fund the *Zero Tolerance for Childhood Tuberculosis* initiative, which will be spearheaded by Mark Lobato in the division. Seed money is being provided to start the Southeastern States Projects and convene the first meeting. DTBE has provided supplemental funds to assure that Study 26 in the TB Trials Consortium can actually be done.

DTBE recently received a specific request from USAID to provide assistance in the Philippines and Brazil. The Coalition for Technical Assistance housed at the Royal Netherlands Tuberculosis Association (KNTB) seeks to provide foreign-

related technical assistance and DTBE is very much a part of that process. Funding is going directly from USAID to that particular group and some ACET members will be asked to provide technical assistance to that effort.

Most recently, Dr. Castro became aware of another CDC office that negotiated an agreement to work in Central Asia, where tuberculosis is a high priority item. The division is deciding how to provide assistance within that context. They have a U.S. Mission in Amat and Kazastan, where they are trying to provide that assistance.

The National TB Controllers Workshop has a new theme of program evaluation. Many of the meeting participants are involved in the planning process and the workshop will be in Danville, Virginia on June 17-18, 2002. A meeting with the Association of Public Health Laboratories to update tuberculosis lab services is being planned. In the early 1990s, the United States did a great job of updating TB laboratories into the 20th century. Now it is time to determine the next steps.

Tuberculosis Morbidity in the U.S., 2001 Data. Dr. Castro presented recent TB data showing a 41% decline in TB from 1992 to 2001 and cautioned the data do not necessarily constitute a trend. The U.S. has averaged a 7% annual decline from 1992 through 2000. From 2000 to 2001, that decline is only 2%. Concerns are that we may be seeing the early aspects of the stagnation and decline of tuberculosis cases and an added effort will be required to keep the curve at the same level. Dr. Castro presented state-specific data only for states with about 100 cases and he noted that some states had increases in reported cases. On average, TB cases are gaining by approximately 5%. Due diligence is needed in these areas to assure that the erosion does not undermine the gains made over the last several years. Dr. Castro said he would welcome ACET's opinion and presented a stratified analysis to show some other trends.

CDC Response to the IOM Report. Dr. Castro focused on the IOM Report and discussed the need to eliminate TB, the CDC response, and the plan. The plan consists of six goals and multiple objectives attached to these goals, as outlined below.

- **Goal 1: Maintain control.**

  Objectives:

  - Maintain and enhance local, state, and national public health surveillance for TB.
  - Support the laboratory infrastructure needed for laboratory-based identification and treatment of TB.
  - Ensure patient-centered case management and monitoring of treatment outcomes becomes a standard of care for all TB patients.
  - Develop community partnerships and strengthen the involvement in TB control.
  - Improve timely investigation and appropriate evaluation and treatment of cough after active TB.
  - Ensure appropriate care for patients with multidrug resistance (MDR) TB and monitor their response to treatment and treatment outcomes.
  - Maintain infection control precautions for health care facilities.
  - Develop improved engineering and personal protective techniques to prevent TB transmission.
  - Improve TB control in foreign-born populations entering or residing in the U.S.
  - Educate the public and train healthcare providers to maintain excellence in TB service delivery.

- **Goal 2: Accelerating the rate of decline.**

  Objectives:

  - Increase the capacity of TB control programs to implement targeted testing and treatment for high-risk populations.

- Promote appropriate regionalization.
- Characterize circulating strains.
- Develop the capacity to respond to outbreaks, with the following aims:
  - Increase the capacity of tuberculosis control programs to implement targeted testing and treatment for high risk populations.
  - Promote appropriate regionalization of TB control activities in high, intermediate, and low TB areas of the country.
  - Characterize circulating strains of TB using fingerprinting methods.
  - Develop national, state, and local capacity to respond to outbreaks of TB.

➢ **Goal 3: Develop new tools.**

Objectives:

- Develop a coordinated plan for TB research as called for by the IOM. This objective needs to be done in cooperation with other federal agencies, particularly NIH and FDA, which are conducting microbacteriology.
- Develop news methods to diagnostic persons with latent TB infection and to identify infected persons who are at high risk for developing active TB.
- Develop and assess new drugs to improve TB treatment and prevention.
- Develop a new and effective TB vaccine.
- Develop and implement a research program on behavioral factors related to TB treatment and prevention.
- Rapid transfer of findings from research into practice.

➢ **Goal 4: Increase the role in global efforts.**

Objectives:

- Provide leadership in public health advocacy for TB prevention and control.

- Provide technical support and build capacity, especially in countries such as Mexico, Philippines, Vietnam, India, and China that contribute significantly to the burden of TB in the U.S.
- Develop models for the diagnosis and treatment of patients with MDR-TB, especially in those countries designated by WHO as "hot spots."
- Provide technical, programmatic, and research support aimed at reducing the incidence of TB in high HIV-burden countries.

- **Goal 5: Mobilize and sustain support (this IOM recommendation has been split into two recommendations by CDC).**

  Objectives:
  - Mobilize support with the goal of developing and implementing health communications campaigns.
  - Help the community foster nontraditional, multisectoral, and public-private partnerships to improve effective and thorough communication activities with particular attention to the appropriate material.
  - Support the development of state- or area-specific TB elimination plans that contain communications activities and build support for TB elimination.

- **Goal 6: Track progress towards elimination.**

  Objectives are as follows:
  - Develop innovative analyses for surveillance data to help focus on elimination efforts.
  - Develop novel indicators of progress toward elimination.
  - Conduct periodic evaluations of program performance at federal, state, and local levels.

The report has been prepared in consultation with TB Controllers and has been shared with ACET members for comments in the past. It is ready to be rolled out now to be given to those who are going to determine what it will take to eliminate

tuberculosis. The report is complementary to the federal action plan that has gone to many government agencies that are part of the federal task force.

Action Item. Dr. Castro assured ACET participants that they will receive a copy of the report in desktop, galley, or final form.

Discussion. In response to a question regarding TB budget cuts, which might occur because of decreases in reported cases, Dr. Castro commented that the effort now is to push ahead with the harder-to-reach populations and do a better job with foreign-born TB elimination. Elimination will not be achieved by a decrease in levels of funding. Flat funding is essentially a decrease because funding is not keeping up with cost of living.

Dr. Masae Kawamura asked about low incidence projects – how much is being allocated to those projects and to what kind of projects, and how much funding will be available to low incidence areas as opposed to low incidence states?
Dr. Castro explained that the eligibility criteria in low incidence states is limited so that large states with recognized low incidence counties will not draw the resources away from states that have not received any resources. Over time this issue will need to be addressed to eliminate TB. The specifics are to explore the possibility of regionalized approaches to proper response to outbreaks, potentially for fingerprinting.

Dr. Kawamura noted the problem of funding going to low incidence states when other areas have higher morbidity. She said what is most important in low incidence states is contact investigation, accountability, and responsibility for case management. Dr. Castro said one potential approach is to have regionalized oversight to provide that level of accountability. The potential for a regional approach is much more efficient than having everything happen from Atlanta, which is the typical approach when responding to outbreaks. Dr. Anne Fanning said this is a good response to the IOM report. Tracking of these goals

is critical, and Dr. Castro said these modest resources need to be concentrated in low-incidence areas and these are not necessarily resources that are being pulled away from the other things. He noted that the program needs to be able to respond to inquiries about how funds are spent. The small increase this year forces tough funding decisions. Dr. Jim Pearson echoed Dr. Fanning's comments regarding funding to low incidence states and said you have to accept that this funding is money well spent to prepare for the next step in TB elimination.

Dr. Lee Reichman said it is not always in the interest of community to have the information that is presented by Dr. Castro presented as good news because funding could be eliminated. He suggested that perhaps NCET should put out talking points to the community. The same talking points can be used when an outbreak occurs. Dr. Castro noted that in World TB Day activities, the Office of Communications delivered a tempered response.

Dr. Charles Wallace agreed that it is critical to have continued vigilance with low-incidence areas to ensure an infrastructure is in place to contain the morbidity and try to prevent an increase in cases. He said it is wise to invest some resources into low incidence states.

Binational Health Card Update: Dr. Castro said the Binational Health Card has been approved by Secretary Thompson and Dr. Julio Franko, the Mexico Minister of Health. What is really needed and what we are working towards is a state information system to approve care and therapy for patients diagnosed on either side of the border, who cross over after diagnosis is made and tend to get lost for followup in the process. An existing system such as Cure TB or TB Net and toll-free numbers will likely be used. Obtaining a toll-free number on the Mexico side is a difficult, but not insurmountable, problem. All parties agree that the so-called TB card should carry minimal information; however, details on how to keep the information on the card updated have not been decided. Mexico's

Mission USA has provided generous resources for this project. There are constraints on use (cannot be used in U.S, only Mexico). The U.S.-Mexico border is another priority area for resources.

Dr. Charles Nolan made a general comment about the impact of the recession in the economy on public health departments in states without state income tax. He raised the issue that states are forced to depend on the federal budget for TB control funding.

Dr. Castro said they have never been able to get a good assessment of state expenditures on TB, thus it is difficult for CDC to report what the country as a whole is spending on TB. If National TB Controllers could gain access to this information independently, it would be very useful. There is a risk of further supplanting modest increases in southeastern states and of the states using federal money to do locally what the state would have funded otherwise. Ms. Sue Etkind commented that spending is very hard to track because money is incorporated into other programs in different ways.

Position Paper on Impact of the Recession on Public Health. Dr. Valdiserri suggested an approach whereby an organization like ASTHO or NACHO might develop a broad position statement on the impact of the economic recession on state-level public health spending, rather than just on TB nationally. This approach will not replace the need for state level data but it might be worth pursuing. Dr. Bailey said ASTHO could be asked to provide this position statement. They have made policy statements before and have had general agreement with the ASTHO/NACHO boards around broad issues. She also thought the National Council of Rural Health might play a role in addressing the needs of rural counties.

Action Item. Dr. Jim Pearson and Dr. Bailey will communicate with ASTHO and NACHO on the issue of trying to get additional information on the impact of

the economic recession on public health indicators. They will indicate that ACET is specifically interested in the impact on TB, but perceives this to be a larger issue. The ACET Chair will write a letter to the Executive Directors of each organization requesting additional information.

Dr. Nolan commented on the response to the IOM Report saying it is very lengthy and ambitious, and evaluation of it will be highly important. He suggested ACET review it annually. Dr. Castro thought a more appropriate plan might be for ACET to devote one meeting session exclusively to evaluating and monitoring progress on the plan. Dr. Anne Fanning said the response has enormous goals that will be difficult to fund and track at the state level. Dr. Valdiserri commented that the plan is necessarily comprehensive and it is important to agree to some key indicators to monitor the plan. Then ACET can use these indicators to give feedback to policy makers. The next step, which is quite challenging, is to agree on some key indicators. Dr. David Cohn said an evaluation of this incredibly comprehensive plan is beyond the scope of ACET, which only meets three times per year. Ms. Etkind said one recommendation of the IOM report is that DHHS should periodically review the status of the recommendations. If this is the CDC response plan to the IOM report, then CDC has to take the next steps in terms of what those key indicators are and how they are going to measure progress. Those are the things that should come back to ACET for review, but the committee should not be the evaluators, per se.

Under goal 4, tracking progress towards elimination, the first two objectives are to develop innovative analyses for examining surveillance data to help focus on these efforts, and to develop novel indicators of progress towards elimination. Dr. Castro suggested that the first order of business might be to come back to ACET for these indicators to decide whether they would be a good measure. He asked for comments on an alternative approach if the council is not the right venue.

Ms. Rachel Stricof said, from the state perspective, it is very important to know what those measurable indicators are and assure that everyone has buy-in. CDC should work with National TB Controllers and others to define the measurable indicators. Another suggestion was to have a working group composed to hammer out some basic measurable objectives to bring to ACET to respond.

Mr. Warren Hewitt said prior to talking about indicators, we ought to talk about the cost of these goals. He noted that since September 11, funds are being allocated to bioterrorism and competition for dollars is even tighter.

Dr. Stephanie Bailey said the response gives the broad goals and the objectives without the measures; now steps to get to the objectives have to be determined. Dr. Nolan asked Dr. Castro if ACET could have a presentation on proposals for evaluation at the fall meeting. Dr. Castro replied that in the interim he would welcome thoughts on what could be the properties or criteria of the indicators that would be used to measure progress. Dr. Anne Fanning said this is an ideal time to revisit the question of funding, which is one of the main indicators and something that state controllers could be asked to try to estimate so you have something against which to measure change.

GPRA. A discussion ensued about whether the Government Performance Results Act (GPRA) has indicators that would be appropriate. Almost every operational unit at CDC has GPRA indicators. Ongoing efforts have focused on making sure that a program does not have multiple sets of indicators for different purposes. Dr. Castro discussed the GPRA indicators for DTBE; one is annual incidence and rates, one is on treatment of cases—percent completion of treatment and percent completion of treatment for contacts. The last two are beginning to be revised because one indicator, which was a process measure, is outdated and will be replaced with a more meaningful one. The new indicators can be consistent with the indicators listed in the *CDC Response to the IOM*

Report. Dr. Castro said the problem with the GPRA performance results is that they are insufficient to measure progress to elimination.

Mr. Warren Hewitt reiterated that GPRA is not the best of all statutory authorities but it is the one that is normative to all government programs and the administration will be using GPRA indicators to decided program funding.
He said programs cannot afford to be evaluated based on indicators that don't fully represent what needs to be measured. The tuberculosis indicators in GPRA address incidence, prevalence, and some of the normal things seen in public health, but they do not address TB elimination. All government agencies are in the midst of revisiting their GPRA indicators as a function of the every three-year requirement. It is incumbent on ACET to take this opportunity to think about whether those indicators should be coordinated more systematically with TB elimination activities.

Action Item. ACET requests the Executive Secretary, Dr. Valdiserri, to provide council members with a current draft of the *CDC Response to the IOM Report* for purposes of offering suggestions on indicators.

Coinfection and referrals. Mr. Hewitt mentioned that many injection drug users with tuberculosis are coinfected with HIV or hepatitis and asked if that could be a position of strength, i.e., to argue that these populations suffer multiple disease entities—not just tuberculosis. Dr. Castro said this topic was discussed at the World Congress on TB the prior day. It is very appropriate to frame the cost of tuberculosis elimination within the context of all the other issues with which these individuals are confronted. In the clinic, however, tuberculosis is often the least of the problems for coinfected patients. These individuals will be followed in the clinic for at least six months and sometimes longer—as much as two years. By establishing the appropriate referral mechanisms during that time, what can be done to improve these patients' health beyond tuberculosis treatment? First and foremost, patients need to be taken through a complete course of tuberculosis

therapy and, in the process of doing so, that very often means facilitating access to housing, rehabilitation programs, etc. When programs see tuberculosis as advancing the broader public health agenda, they clamor for those programs to be there.

Interim Guidelines on QuantiFeron®-TB Testing (QFT). Dr. Rick O'Brien thanked the Council for the opportunity to present information on the QuantiFeron®-TB (QFT) test and to discuss the draft guidelines on its use that CDC hopes to issue later this summer. The test was approved last year by the Food and Drug Administration (FDA) as an aid for the diagnosis of latent TB infection (LTBI). This approval was, in part, based on two clinical studies, one conducted by CDC and the other by the Walter Reed Army Institute of Research (WRAIR) that compared the QFT test to the tuberculin skin test (TST). In June 2002, Cellestis Limited, the Australian company that produces the test, opened an office in San Diego for marketing and distribution of the product.

The QFT test is based on the production of gamma interferon from lymphocytes that have been sensitized in response to tuberculosis infection. Heparinized whole blood is incubated in four separate wells with mycobacterial antigens (PPD-tuberculin and an *M. avium* sensitin), a mitogen (positive) control, and a negative (nil) control. The resultant interferon gamma in the plasma is measured by ELISA. Results are available within 24 hours of blood draw, and test interpretation is based on measurements in all four samples.

Data from the CDC study showed 84% agreement between the QFT test and the TST, with TST having a slightly higher rate of positivity. The WRAIR study yielded similar results. Older data from an Australian trial suggest that the QFT test may more accurately identify LTBI than the TST.

Proposed Guidelines. The primary topic for this presentation was the draft guidelines that have been developed in consultation with tuberculosis experts at

three separate meetings in North America this year. It is proposed that the test could be used in initial screening for those at low risk for LTBI (e.g., military recruits), where a higher cutoff would be used to define a positive test. A positive QFT test would also require confirmation by TST before treatment of LTBI is considered. If the TST is negative following a positive QFT test, the TST should be repeated in three months. ACET participants raised concern about establishing a baseline readout with the QuantiFeron®-TB Test and whether we know what a QFT conversion looks like. Dr. O'Brien said this issue will be addressed in a study that is about to begin.

Another category of persons for whom QFT testing might be considered are those who are at relatively low risk of LTBI but will have ongoing periodic testing, such as health care workers. Again, a stringent cutoff will be established for an initial positivity and a confirming skin test will be done prior to starting treatment. An ACET participant suggested caution in wording this recommendation to avoid the appearance of suggesting excess testing under low prevalence conditions.

Contraindications. The QFT test is not recommended for the diagnosis of M. avium infection or disease. It should not be used as a diagnostic aid for persons with suspected active TB until more data on its performance in TB patients are available. The test is not recommended for use in contact investigation; this will be the focus of a study that will begin shortly. The test is not recommended for the evaluation of persons with radiographic evidence of prior TB (Class IV).

Remaining Study Questions. A question yet to be addressed is the affect of the TST on the QFT test. The QFT should be further evaluated in screening immigrants from high-incidence countries. DTBE, together with the Division of Migrant Health and Quarantine, recently initiated a study of the QFT test in Vietnam, testing both prospective immigrants and persons with suspected active tuberculosis. The test has not been assessed for use in infants, children, pregnant women, and other high-risk groups.

Cost. The test will cost $10.00 in kit form and the lab test will cost approximately $15.00. So the total cost will be a minimum of $25.00 and a maximum of whatever the laboratory might charge.

Discussion. Ms. Stricof said the New York Department of Health is probably likely continue new CDC-recommending baseline testing for healthcare workers, so relying on a whole blood test that will not elicit boosting is a better idea than planting a tuberculin skin test. She expressed surprise that CDC is not proposing to recommend the test for evaluation of TB contacts. In a contact investigation, an immediate skin test is done and, if negative, it is repeated at 10-12 weeks. However, it is not possible to distinguish between boosting and new infection for those whose repeat test is positive. With the QFT test they may be able to make that distinction because they would not be eliciting boosting.

Dr. O'Brien said CDC is delaying recommendations on the use of QFT testing in contact investigations because 1-2% of contacts have active TB, and there are concerns about the performance of the test in those with active tuberculosis. Ongoing studies in TB contacts and TB suspects should answer these questions. Ms. Stricof noted that using the tuberculin skin test as a diagnostic tool is problematic because one-in-five non-HIV infected people test negative on tuberculin skin testing. Dr. O'Brien said that commonly such patients have advanced and HIV immunosuppression and may also have false negative QFT tests.

Discordance. An issue was raised about discordance, what it means, and the absence of a gold standard. Dr. O'Brien said discordant results should not be an important issue because the guidelines do not propose routinely administering both tests. In a low risk population, the rate of discordance will only be about 5%. The guidelines will suggest that the practitioner evaluate the relative

contribution of both tests and make a decision in cases of QFT-positive, TST-negative persons. One option would be to repeat the skin test in three months and those who remain TST-negative and QFT-positive will not be considered to be infected. The risk to progression to active TB in TST-negative, QFT-positive persons is not known, and the cost benefit equation for LTBI treatment may shift radically. Dr. Castro suggested caution in recommending use of the test in contacts until further studies have been completed. Also, CDC's latest guidelines for targeted testing run against the very first recommendation, which is to use QFT in low risk groups. Current recommendations are that low risk groups do not need to be tested, but they will be tested because of mandates by schools, hospitals, etc. The language needs to be carefully drafted to avoid the impression that CDC recommends testing in low risk populations just because the QFT test might be better than the TST.

Meeting participants decided the issue of discordance needs further evaluation but should not prevent issuance of guidelines because the test is on the market and people are anxious to use it.

Action Item. Dr. Nolan suggested that ACET members have the opportunity to review and comment on the draft guidelines prior to submission to the MMWR, and Dr. O'Brien indicated that this would be done.

Update on the CDC Response to the OSHA Rule Reopening.

Dr. Greg Wagner updated the committee on the *CDC Response to the OSHA Rule Reopening*. He summarized the comments that CDC prepared in this response. In 1997, OSHA proposed workplace standards for protecting healthcare workers against tuberculosis. The comments OSHA received following publication of their draft standards questioned the adequacy of their response to risk assessment. In June, 1999, two new draft risk assessments were peer-reviewed by distinguished scientists. At the same time Congress mandated funding of an IOM committee to explore TB in the workplace and

answer specific questions. That committee included ACET members and other consultants. The IOM findings were reported in 2001. In January, 2002, OSHA reopened the rulemaking record, acknowledged the existence of the IOM report, and asked for comments on their risk assessments.

The IOM findings for control of TB risk in health care settings were that tuberculosis remains a threat to some healthcare workers. The CDC recommendations for TB control were that an OSHA standard can have a positive effect, particularly if it is consistent with the control measures that have been found to be effective, if it increases compliance with those effective measures, and if it is flexible in matching the efforts and controls to the level or risk. The IOM Report also noted a variety of data gaps, research needs, etc.

The IOM report referred to respirators and CDC knew that OSHA had an interest in additional information, particularly on the issue of fit testing. The comments reflect the fact that alternate procedures are not yet ready for implementation. They have not been developed and until they are, the recommendation remains for fit testing to assure both adequate training and protection of workers. On the specific issue of periodicity, CDC wanted to notify OSHA that a specific exception to their annual testing requirement might be warranted and they should examine the nature of the evidence, particularly of the effectiveness of the CDC guidelines to date.

Overall, CDC found the draft risk assessment to be an improvement over the original risk assessment prepared in 1997; however, it still warrants revisiting and needs revisions. OSHA used two primary data sets, one old and one more recent. CDC supported the continuing use of both data sets as reflective of TB risk at different times. Concerning death and reactivation rates, CDC noted that death rates are falling and provided additional data from surveillance information that was not available to OSHA at the time they put out their risk assessment and noted the continuing downward trend. After looking at the data, CDC had some

additional evidence that OSHA had not considered and CDC recommended the use of a 3-5% reactivation rate.

In summary, CDC presented a consensus set of comments continuing to support the OSHA effort to improve the protection of workers from TB and noting, as did the IOM report, that the standard should be flexible, should allow for improvements as CDC guidelines change, and that the risk assessment as currently presented should move forward. OSHA closed its record on May 24, 2002 and this remains on their regulatory agenda. The CDC revised guidelines are expected to be published prior to any final rule by OSHA.

After a few brief comments about respirator fit issues, Dr. Michael Tapper acknowledged all the parties are involved in creating this response. Dr. Castro noted that the new imperative of having personal protective devices such as respirators available in case of bioterrorist threats will push the market to develop better devices.

Progress Report on TB Genotyping Manual. Dr. Scott McNabb gave an update on the work the division has been doing on developing guidelines for the use of DNA fingerprinting. As a brief background, CDC funded seven regional laboratories and sentinal surveillance sites and conducted a perspective study between 1996 and 2000. In that prospective study, incident culture-positive TB case patients were enrolled within each of the seven catchment areas. Almost 12,000 patients enrolled in the study. The study employed standardized protocols for fingerprinting of the isolates from these patients, and for gathering certain epidemiologic outcomes. The information is being prepared for publication in the scientific literature and as a document that can be used in the field by health intervention specialists. Plans are to measure findings from National Tuberculosis Genotyping Surveillance Network (NTGSN), which was published in a special issue of the *Journal for Emerging Infectious Diseases*. Fifty-five manuscript proposals were received from the NTGSN members; 30 of

those have been accepted and 24 of those have been through second editorial reviews and are ready for submission to the journal. Six manuscripts are still in the preparation phase. The original deadline of June 3, 2002, for an October 2000 publication date was been pushed back one month so the current deadline for the final submission of these 30 manuscripts is July 1, 2002. These manuscripts will then go out for peer-review. CDC is charged with analyzing this national data set with papers that will come out and will be separate from the special issue. Dr. McNabb noted that out of this framed discussion, it is nice to have all of these scientific papers published; however, he questioned their relevance to someone who is working in the field?

Dr. Zachary Taylor, in fact, challenged CDC to think about how we might translate some of this scientific information into a practical means that could be used by TB Controllers and those who are working in the field. The conceptualization and development of the handbook proceeded from these discussions. The justification for the handbook is that it translates highly technical information into a usable format to provide practical guidance about fingerprinting and its limitations.

Through collaboration between NTCA and CDC, controllers and those working in the field can be given a basic foundation of knowledge about fingerprinting. Thus, CDC established collaboration with the National TB Controllers Association, separating roles and responsibilities. The roles of NTCA were to facilitate development of a needs assessment, which CDC conducted last year, and to collect the data from that needs assessment. CDC's roles were to facilitate the project development and planning, provide technical assistance for the needs assessment, and analyze and present the data.

Dr. McNabb elaborated on the handbook working group, the steps in handbook development, the handbook format, and the purpose of the needs assessment, which is to determine the knowledge levels of TB Controllers and their staff,

current levels of use of DNA fingerprinting, and the optimal educational format for a handbook. The current status of the handbook is that the detailed outlines are complete and the authors are working on the first draft of their particular sections. The handbook is slated for November 2002 publication to coincide with the *MMWR* special issue that will be released at that time.

Discussion. A comment was made that the handbook should add a few paragraphs on TB control in developing countries. Dr. McNabb said the working group has tried to develop a document that is not too specific because of changing technology and change in circumstances. Dr. Castro suggested the additional of language or a section to be shared with those who have been using fingerprinting in the international community and said it is not wise to unilaterally draft the final language without input from those who will use it. An ACET participant said the handbook will be an excellent tool for understanding retrospectively how TB is transmitted; however, it will not facilitate real time traditional contact followup. The limitations section of the handbook acknowledges this issue. Dr. Charles Wallace said the field needs a 'DNA Fingerprinting for Dummies' handbook to understand the process well enough to apply it to practice.

Dr. Castro asked for ACET's input on how to distribute *MMRW* recommendations and special reports on fingerprinting. An *MMWR* forum might not be appropriate because the potential is much smaller. Dr. Castro said labs, epidemiologists, and health officers outside of the TB community are unaware of DNA fingerprinting. Having it in this format raises awareness and informs people who are often going to be making decisions as to whether or not to fund or support fingerprinting. A comment was made that molecular fingerprinting is beginning to be used in so many different areas that any primer will be beneficial if it brings together those who are ultimately going to use the data. Any input ACET wants to provide would be very welcome. Dr. Tapper said there is a parallel mandate from ACET about how to approve laboratory services for CDC. CDC has been

working closely with APHL and a broad framework that Jack Crawford presented at the last ACET, and fingerprinting is a part of that. He updated CDC on a number of activities last time that are occurring in that direction.

In summary, Dr. McNabb said there are still some important research questions that need to be asked and answered. One of the tasks of the new consortium addresses some of those questions about fingerprinting. Plans are underway for operational research to be conducted in the future through the new CDSD consortium.

Riboprinter. Dr. Denise Toney presented a report on TB genotyping. Two years ago, the Virginia Public Health Laboratory initiated efforts to perform DNA fingerprinting on every single isolate that was identified by the lab with hopes that, as with other organisms, with routine surveillance we may be able to more rapidly identify the beginning onset of clusters of disease. Routine surveillance data could be communicated that information to an epidemiologist and hopefully, have an impact on further transmission of disease.

A variety of methodologies exist for subtyping of organisms. Prior to implementation of molecular biology techniques, laboratories employed phenotypic methods such as biological or biochemical properties of the organism, as well as drug susceptibility profiles. With the implementation of molecular biology techniques, laboratories have transitioned to the use of these methodologies because of their speed and sensitivity, and because of being able to exact very close comparisons between organisms.

Dr. Toney outlined the techniques that may be employed for molecular typing to TB and focused on DNA fingerprinting, which has been the most widely used technology for comparison of TB strains. She presented a simplified version of DNA fingerprinting. She described work that her agency employs at the Division of Consolidated Labs for DNA fingerprinting. They began doing manual typing,

then switched to a more innovative approach that allows automation and makes it easy to do at the public health laboratory. In collaboration with the health department, they decided to do DNA fingerprinting and evaluated all the existing methods to determine the best approach. They decided to pursue using restriction fragment link polymorphism (RFLP) analysis because it is the gold standard. Because of the intensive labor demand, they decided to evaluate the ability of an automated system and chose the characterization system that can do fingerprinting. This is very cost effective because it requires little personnel time. Dr. Toney detailed the process used to evaluation the capabilities of the riboprinter and said they are very pleased with the results of this automated DNA fingerprinting technique.

In conclusion, the automated system provides clear and reproducible fingerprint patterns that can be obtained in about eight hours from the time of DNA isolation. The fingerprint patterns are comparable to those generated manually; although manual fingerprinting gives better resolution. Using software, they are able to bulk analyze the data to identify clusters, trends and fingerprint profiles. From the examples given, it appears that this technology, even though it has less resolution, is able to clusters organisms that are supported by epidemiology and identify clusters that can initiate additional investigations on behalf of the health department.

Update on TB Treatment of Persons in INS Custody. Dr. Masae Kawamura updated ACET on the TB MMWR article on Treatment of Person in INS Custody. The latest draft of the document entitled '*Issues Concerning Completion of Tuberculosis Treatment for Persons in Custody of the Immigration and Naturalization Service*' was being submitted for clearance just after the February meeting; however, a very important comment and suggestion came from one of the workgroup members, Dr. Wallace, so the issue was taken back to the workgroup. They decided the issues were important and should be included. A third vignette was added. The rest of the document is relatively

unchanged, except for some data updates in the first paragraph. The recommendations that ACET approved at the February meeting are included in the document. A word limit may result in one case being eliminated. A time period for ACET to comment on the document needs to be set.

Action item. Any final comments should be submitted to Michael Lademarco (and copied to the working group chair) within a week and members should note that this document is going through internal clearance.

Tuberculosis in the Southeastern United States. Dr. Stephanie Bailey is the Chair of the work group focusing on TB in the Southeastern United States. The SE United States work group had a conference call which generated several ideas about future focus. In February, 2002, DTBE committed to an *MMWR* on the issue of ethnic and racial health disparities regarding tuberculosis and the unique infrastructure issues in the Southeastern U.S. Dr. Castro suggested that a journal article might be preferable to an *MMWR* article.

Dr. Bailey said the work group is seeking direction and is thinking of convening a technical consultation to bring stakeholders and experts together to assess their role and develop a research agenda. The work group is interested in convening this meeting as an adjunct to another meeting, possibly a meeting being convened by Dr. Zachary Taylor or during a meeting held by the Public Health Foundation on community-based activities relative to TB. There is a lot of interest in looking at what community-based activities are happening, the best practices, and enhancing those roles to deal with TB issues at the community-level. Dr. Bailey said the SE TB Controllers group is also considering best practices and what has worked in the community.

Dr. Valdiserri said staff could provide details about Dr. Taylor's meeting, which would be similar in focus, though not a complete overlap. Dr. Castro said it is a planning meeting for those who applied and obtained resources under a Request

for Proposal (RFP) to develop interventions to deal with the tuberculosis in the SE states. Dr. Valdiserri said that it might be too much to add to the agenda of a predetermined grantees meeting.

Dr. Theresa Watkins-Bryant said the Department of Health and Human Services has become very interested in health disparity reduction issues and has asked HRSA to make a presentation to Secretary Thompson regarding health disparity reduction initiatives that are in place. As such, framing TB issues in terms of disparity issues would probably be appropriate.

Dr. Fanning said the IOM goals can be used to structure addressing the southeastern states' issues under the categories of those goals. People who are looking at the issues should not be separated from those who are potentially doing research projects on the same issues. Dr. Bailey said the goal is to do practice and research and they are not exclusive of each other.

Dr. Wallace commented that the work group's second meeting should bring together stakeholders, review what has happened in the past, and start developing systems for the future. A thorough literature review should be done as well. When stakeholders meet with funded project leaders they can set the stage for the future. HRSA has a lot to bring to the table in this process because they are mandated by their mission to do activities that will make a difference in the overall profile of health disparities in the African-American community. Dr. Nolan suggested that Terry Watkins-Bryant, who is the new ACET liaison member from HRSA, be recruited to work on this. She agreed. Dr. Bailey said she is hearing that it is important to inform stake holders and get the message out through journal articles, poster sessions, and conferences. Looking at community-based interventions prompts emerging questions and knowledge for further research on this topic, which could begin to create the research agenda. After the information is made public, a meeting should be planned where people present information to create political will and community strategies. If you

create the political will, resources will be provided to go towards elimination and addressing the issues with some unique strategies.

Action Item. Mr. Hewitt said he would discuss this topic at the next Black Caucus Meeting. He said TB is a relevant topic for this meeting because incidence in African-American communities is rising.

Dr. Watkins-Bryant mentioned that ABC is dedicating free radio time to talk about issues that directly affect the African-American community and that might be an appropriate forum for this discussion.

Dr. Valdiserri summarized the discussion into two issues. The first is that the workgroup wanted to ask ACET its opinion of bringing together stake holders for the purpose of identifying best practices and raising awareness. ACET members agree that to raise awareness, the information needs to be put into the public domain. Suggestions are an *MMWR* article (word count might be limiting) or a journal article (speed of publication time is an issue). Several suggestions were made about the Deputy Secretary's upcoming meeting. Dr. Valdiserri suggested a query to get specificity and clarity on the meeting that ACET and CDC should hold and he questioned what should be the main focus—raising awareness and/or identifying best practices or whether those are actually separate activities. The second issue is that Dr. Bailey wants specificity on what the workgroup should focus on next.

Dr. Nolan said he envisioned this work group as the next in a line of specific extensive studies on the part of ACET, such as with the vaccine blueprint, the revisitation of elimination, and TB in low incidence areas. The next one would be TB in the Southeastern United States, with an end product to be a document with recommendations for TB elimination in the southeast and perhaps among African-Americans.

Ms. Stricof said the data should not be limited to the southeast. There are two different issues. One is, what is going on with the epidemiology in the southeast, what is contributing to TB there, and how can TB be controlled it in the southeast. The other is racial/ethnic disparities, which are everywhere and are not unique by any means to the southeast. She asked if the focus is going to be on interventions in the southeast and if those interventions are different because of the way the population is geographically dispersed. Different geographic regions have differences regarding racial ethnic disparities. The two should be separated because racial/ethnic disparities are universal to the country and are not limited to the southeastern states. The goal of the workgroup needs to be defined. It is focused on the southeast to compare whether most TB cases are U.S.-born versus foreign-born, as there are different interventions. Then the racial/ethnic issues could be tackled. Or the workgroup could take on the broader issue of racial/ethnic disparity issues not limited to the southeast.

Mr. Hewitt said the southeast has a very different pattern of racial health disparities than other parts of the country but it can be a microcosm of other areas of the country. It is valuable to explore these issues to understand the extent to which TB falls under the disparity issue. Dr. Kawamura noted that CDC dollars have already been given to urban areas with high incidence of TB; whereas the southeast has not been addressed and the problems are very different. She suggested two stake holder meetings—a task force with experts on tuberculosis to garner ideas and create strategies, and a second meeting to raise awareness and plan objectives based on the strategies that have been created.

Dr. Castro said trends are moving in the right direction and all states except Texas have experienced a decline in TB cases since 2001. In looking at the epidemiologic profile, the rates are highest in U.S.-born African-Americans. Therefore, the challenge is to do something to accelerate the rate of decline. Inevitably the issue will come back to the broader agenda of closing the gap on

racial and ethnic disparities. But the epidemiology is local and what is happening in the southeast may not necessarily be the same as what is seen with racial and ethnic disparities in northern parts of the country. The case that TB is part of that broader problem needs to be convincingly stated. An important decision for this workgroup is to see whether recommendations for a consultation are consistent with a planned meeting. If so, the meetings should he held simultaneously. If they diverge, separate meetings are needed. Given that the division is going to be sponsoring a meeting on the RFA results sometime in late August; if ACET has a list of items it wants out of the consultation and they happen to match what is being done for another related reason, then one meeting should combine both efforts.

Dr. Valdiserri noted that a grantees post award meeting may not represent all the grantees and stake holders and if you bring other stake holders in, it could be disruptive for the grantees. The working group should let the division know if there are particular issues that they would like to share with the grantees at this meeting and one or more representatives of the working group can participate in and observe the meeting. He suggested that ACET hold a separate stake holders meeting to make the leadership of the African-American community more aware that the TB issue is important. This meeting could be jointly held under the auspices of ACET and CDC. Another option would be to use some doctors from those areas and work with them and through them to convene a community-based meeting. One comment was made that TB issues should be linked with typical coinfections such as HIV, and TB should be a component of meetings on those coinfections.

Action Item. It is the strong consensus of ACET to support this work group initiative. Dr. Bailey was told to move forward with the suggestions that have been made. A representative from ACET should attend the August work group meeting and report back at the next ACET meeting.

Community-based TB prevention projects. Ms. Sue Etkind substituted for Dr. Patrick Chaulk and provided an update on community-based TB prevention projects. Her involvement is not as part of the NTCA. The history of this interest in community-based TB prevention came about as a result of discussions between Dr. Chaulk and Ms. Etkind at the IOM meetings, where the focus was on TB elimination and there was discussion about community-based prevention. They took it up as a mission to explore community-based TB prevention efforts and see if there was a way to get the message out about community-based prevention, what is being done, and what can be learned from it as part of the national agenda.

Dr. Chaulk subcontracted with the Public Health Foundation to do a literature review relative to community-based TB prevention to identify key areas already involved in it. The literature review did not yield much information that was TB-focused, so they decided to put the literature reviews they found into a compendium publication as a start. From the few that were found, the Public Health Foundation targeted ten sites and began interviewing people at those sites. The interviews are complete, an outline report has been written, and an Executive Summary will be produced. The report talks about latent TB and the country at a glance relative to latent TB trends. The information is being presented in case stories that examine individual community-based programs, spotlight on the various programs they have picked, define the problem, describe how target groups were identified, and what kind of community involvement took place. They will talk about what the goal was for each of these programs and how the goals were achieved in terms of funding, personnel, leadership, and advisory steering committees. The types of interventions such as education, screening, and treatment done at the various sites were explored. The report will discuss outcomes and lessons learned relative to funding sources, sustainability, governments, and policy indications of these kinds of programs locally and statewide. Then the report will present recommendations relative to the importance of culture, community, and other issues related to community-based

testing. It was suggested that Dr. Chaulk be invited to the next ACET meeting to report on the progress of this project.

Discussion. A question was asked about how 'community' is defined in the context of this project. Ms. Etkind said for the purposes of this project, community was not defined geographically. The communities targeted ethnic subpopulations within areas where someone identified an interest. Mr. Hewitt noted that definitions of 'community' are an ongoing problem. When talking about racial and ethnic communities being served, the serving entity does not have to be indigenous to the community or composed of racial and ethnic people. We are constrained about using the logical definition of community because of issues about equitable expenditures, dollars, and constitutional guarantees.
Dr. Wallace and Dr. Bailey noted that the scant literature review is not surprising, in part because those who are working in the communities are often too busy to publish. Dr. Wallace also noted that the most knowledgeable source in the community is not necessarily an organization; it could be a person who is indigenous to the community and knowledgeable about what is happening in the community.

Action Item. ACET will invite Dr. Chaulk to its next meeting to present the perspective of the Public Health Foundation in this effort.

The ACET Chair entertained a motion to accept the previous meeting minutes; the motion was so moved and properly seconded by voting members. There were no further changes or discussions. The February 2002 ACET meeting minutes were unanimously approved.

Closing Session. ACET voted to set the next meeting date for November 7-8, 2002. There being no further discussion, Dr. Nolan adjourned the ACET meeting at 3:15 p.m. on June 6, 2002.

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I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.

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Charles M. Nolan, M.D., ACET Chair Date: _____